



National Institutes of Health  
National Cancer Institute  
Bethesda, Maryland 20892

**DATE:** July 28, 2009

**FROM:** S. Percy Ivy, M.D., Associate Branch Chief, Investigational Drug Branch, CTEP, DCTD, NCI

**SUBJECT:** Oxaliplatin (Eloxatin), NCI IND Safety Report, AE# **1265048**

**TO:** Investigators Using Oxaliplatin, NSC 266046

The U.S. Food and Drug Administration (FDA) regulations require sponsors of clinical studies conducted under a U.S. IND to notify the FDA and all participating investigators of any serious and unexpected adverse experiences that are possibly related to the investigational agent. Please find attached a copy of an IND Safety Report recently submitted to the FDA for the CTEP-sponsored investigational agent oxaliplatin.

The following must be completed by all investigators using oxaliplatin under NCI IND 57004:

- Send a copy of the IND Safety Report to your Institutional Review Board (IRB) according to your local IRB's policies and procedures.
- File a copy of the IND Safety Report in your protocol file.

If your study is not covered under IND 57004, it is strongly recommended that you follow the instructions above.

Please note that for Cooperative Group studies, the Cooperative Group Operations Office will provide instructions for IRB submissions, any patient notifications, etc.

Based on CTEP's assessment of the current information in light of previous experience with oxaliplatin, there does not appear to be a change in the risk-benefit ratio for oxaliplatin studies; therefore, CTEP is not requiring a protocol amendment at this time.

Please continue to report events according to the adverse event reporting guidelines in your protocol(s).

The attached Adverse Events Assessment describes the adverse event(s) (synopsis provided below), relevant previous experience under this IND and/or NSC, and the total number of patients enrolled in trials under this IND and/or NSC:

An 85-year-old female with adenocarcinoma of the colon experienced grade 5 sclerosing cholangitis 2 years after having been on a phase 3 study utilizing the investigational agent oxaliplatin in combination with leucovorin and 5-fluorouracil.



Adverse Event	Grade	Attribution
colitis (n=41)	5	1 Definite
	4	3 Definite, 1 Possible, 1 Probable, 1 Unlikely
	3	15 Definite, 5 Possible, 3 Probable, 3 Unlikely, 1 Unrelated
	2	2 Definite, 4 Possible, 1 unrelated
cholangitis (n=1)	2	1 Unrelated

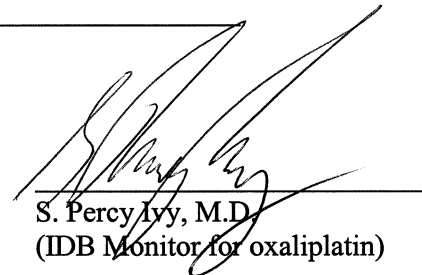
To date, 20724 patients have been enrolled in NCI-sponsored clinical trials under the oxaliplatin IND and/or NSC.

In this case, it is thought that a possible causal relationship between the event and oxaliplatin therapy cannot be excluded.

	<b>Sclerosing cholangitis</b>
<b>Oxaliplatin</b>	Possible
<b>Leucovorin calcium</b>	Unrelated
<b>5-Fluorouracil (5-FU)</b>	Possible
<b>Adenocarcinoma of the colon</b>	Unrelated
<b>Colitis</b>	Probable
<b>Previously elevated liver functions</b>	Definite
<b>Possible emerging immune related colitis/sclerosing cholangitis</b>	Definite

Date: 072809

Signature:



S. Percy Ivy, M.D.  
(IDB Monitor for oxaliplatin)

If this assessment is changed, we will notify your office.

cc: Ron Knight, Ph.D.  
Mark W. Moyer, M.D.  
[GPEmailbox@sanofi-aventis.com](mailto:GPEmailbox@sanofi-aventis.com)  
Sanofi-Aventis Pharmaceuticals, Inc.